

N. J. C. Works

with Dr. Theobald's review

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PATHOGENY OF SYMPATHETIC OPHTHAL-
MIA, VIEWED FROM A MACRO-
SCOPIC STANDPOINT

BY

SAMUEL THEOBALD, M.D.,

PROFESSOR OF DISEASES OF THE EYE AND EAR IN THE BALTIMORE POLYCLINIC AND POST-
GRADUATE MEDICAL SCHOOL; SURGEON TO THE BALTIMORE EYE, EAR,
AND THROAT CHARITY HOSPITAL

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PROBABLY among the members of the Society present this evening there are some who can recall an amusing and not less instructive incident which happened in one of our local medical societies not very many years ago. A patient who had exhibited somewhat obscure symptoms, to obtain relief from her sufferings, sought medical advice. A suspicious-looking mass was discovered blocking up the posterior nares, and was removed without difficulty, having sloughed off, apparently, from its former attachments. The supposed neoplasm being regarded as probably of malignant character, it was, of course, deemed of the first importance that its histological structure should be determined; a portion of the tissue, therefore, was teased out, and submitted to microscopic examination. This completed, the growth was exhibited to the society in question, its histological characteristics were duly set forth, and the clinical facts of the case were related. An animated discussion followed, and more than one hypothesis was advanced to account for the unusual features which the case presented. While this was in progress, an inquisitive individual, with macroscopic proclivities, inspected the tumor with more care, it would seem, than had been previously thought requisite; and the

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debate was presently cut short by the announcement that the suspicious neoplasm was, after all, but a half-digested oyster, a harmless specimen of our should-be-familiar bivalve, which, probably, during a previous spell of vomiting had become lodged at the point where it was discovered.

There is a resemblance, not altogether fanciful it seems to me, between this oyster episode and the study of the pathogeny of sympathetic ophthalmia, as recently conducted by certain microscopists. Intent upon the "threads of fibrin," the "emigrant round cells," and the "microphytal organisms" which their microscopes reveal, these investigators appear to have lost sight of the macroscopic picture of the disease, with which, as clinicians, they should have been familiar, and as a consequence they have promulgated theories regarding its nature which are satisfactory only when viewed from the narrow standpoint of their authors.

Although Mackenzie and the other earlier writers upon sympathetic ophthalmia were disposed to regard the *optic* nerves as the probable route by which the inflammation extends from the primarily to the secondarily affected eye, this view, as is well known, was afterwards universally abandoned, and it was taught by all authorities, among them Von Graefe, Donders, and Bowman, that the *ciliary* nerves are the medium through which the sympathetic influence is transmitted, and that the inflammation in the second eye is not the result of direct extension from the one first affected, but is due to a morbid influence reflected through certain of the nervous centres. In support of this latter view, numberless observations have been recorded: as, for instance, the cases reported by Bowman and by Von Graefe, in which the starting-point of the sympathetic inflammation in the second eye occurred at a spot of the ciliary region which corresponded symmetrically to that at which the first eye had been injured; the numerous dissections, by Donders and a host of other competent observers, of eyes enucleated for sympathetic irritation or inflammation in the fellow-eye, in which the ciliary nerves exhibited signs of inflammation, were found torn, compressed, em-

bedded in the traumatic cicatrix, or subjected to unusual traction¹; and the concurrent testimony of all ophthalmic surgeons, that sympathetic ophthalmia is especially prone to occur as a consequence of injury to those parts of the eye to which the ciliary nerves are chiefly distributed—the ciliary body and iris. So convincing, indeed, was the testimony offered from every quarter, that the mode in which sympathetic inflammation is propagated seemed settled beyond peradventure.

Within the past five or six years, however, all this has been changed, and now, if one may judge by the current literature upon the subject, the pathogeny of sympathetic ophthalmia is the one point in ophthalmology concerning which we are most in the dark, and hold views which are least defined. On the one hand, the disciples of Cohnheim would have us believe that it is impossible for an inflammation to be excited by an irritation reflected through the ciliary nerves; on the other, the germ theorists tell us of septic choroiditis, of microphytic organisms, and of peri-neural lymph-sheaths opening wide for their ready transmission. Now we are assured, in spite of all that we have been taught to the contrary, that in the exciting eye the ciliary nerves are rarely, and the optic nerve and retina almost invariably, the seat of pathological changes; and again we are reminded of the circle of Willis, and of the facility with which alterations in the choroidal vessels of one eye may be transmitted by way of the ophthalmic arteries, the internal carotids, and the circle of Willis to the corresponding vessels of the other.

To whom and to what, then, are we indebted for this astonishing change, for this sudden subversion of views which had been accepted and taught for the last quarter of a century by all the great masters of ophthalmology? If I mistake not, Dr. Adolph Alt, now of St. Louis, is entitled to the credit of having initiated the movement, by the publication, in December, 1876, in the *ARCHIVES OF OPHTHALMOLOGY and OTOTOLOGY*,² of a paper "On the anatomical

¹ Wells' "Diseases of the Eye," fourth Am. edition, note by the editor, Dr. C. S. Bull, p. 339.

² Vol. v., Nos. 3 and 4.

causes and the nature of sympathetic ophthalmia"; in which he gave a description of the pathological changes found in 112 eyes that had been enucleated on account of "sympathetic affection" of the fellow-eyes, and expressed the opinion that the statistics which he had accumulated "strongly sustained" the views of the earlier authors, "that the optic nerve plays a great part in the transmission of sympathetic ophthalmia." The all-pervading influence of the germ theory of disease has also played an important part; and still more important in favoring the change has been the influence of the theory of inflammation at present most in vogue, which regards "molecular alteration of the vascular walls as the indispensable condition for the development of inflammation," and "busies itself but little with the influence which the nerves may exert upon inflammation, or denies it entirely."¹

Let us now consider the data brought forward by Dr. Alt, and see to what extent his conclusion, that they strongly sustain the view "that the optic nerve plays a great part in the transmission of sympathetic ophthalmia," is justified; and this it is the more important to do with care, because his statistics are quoted by all those who oppose the old theory of transmission, and are used as the basis of many of their strongest arguments. It is to be observed, in the first place, that the view he favors is that of *direct transmission of the inflammation by way of the optic nerve itself*, and not by way of the peri-neural lymph-space, as Leber and others have since suggested. Since he bases this conclusion upon the large percentage of "changes" in the retina and optic nerve, and the relatively small percentage of "changes" in the ciliary nerves, which he states the enucleated eyes exhibited, we shall direct our attention more especially to these points. "The percentage of changes in the retina and the optic nerve is remarkably great—79 per cent.," he states, and this he thinks "should engage very earnest consideration—the more so, as there are but $16\frac{2}{3}$ per cent. which present changes in the ciliary nerves."²

¹ "Sympathetic Diseases of the Eye": Mauthner, Am. edition, pp. 109 and 112.

² Page 474, vol. v., Nos. 3 and 4, ARCHIVES OF OPHTHALMOLOGY and OTOTOLOGY.

In attempting to verify these figures, an unexpected difficulty presents itself at the outset, which is significant because of its bearing upon the accuracy of his methods. Although at the commencement of his paper Alt states that his statistics relate to 110 eyes enucleated on account of sympathetic affection of the fellow-eyes, 32 of which had been placed at his disposal by his colleagues, and the data regarding 78 had been compiled from literature, a careful count shows that 112 such eyes are described in the tabular compilation (80 derived from literature). His percentages, however, are based upon a total of 110 cases. Accepting the data *as given in the tabular compilation*, we find, as regards the ciliary nerves, that in 66 of the 112 cases no mention is made of their condition. In these cases it is probable that no attempt was made to ascertain whether they had undergone pathological changes or not; for, though one may cut open an enucleated eye, and detect at a glance the existence of detachment of the retina (and this condition, as we shall presently see, constitutes a very large part of the "retinal changes" to which so much importance is attached), a much more elaborate examination, involving usually the making of microscopic sections, is necessary to determine whether the ciliary nerves are the seat of pathological changes.

Disregarding, therefore, these sixty-six cases, and taking account only of the forty-six cases in which the condition of the ciliary nerves is mentioned, we find them described as "normal" thirty-one times, as presenting pathological changes of histological character six times, gross pathological changes (torn, compressed, lying in tissue of scar, etc.) seven times, both histological and gross pathological changes once, and "not discoverable" (apparently having been entirely destroyed) once. Considering the condition of the nerves in this last case as pathological, we have fifteen cases presenting either histological or gross pathological changes in the ciliary nerves in a total of forty-six, or 32.6¹ per cent. instead of 16 $\frac{2}{3}$ per cent. as given by Alt. The

¹ In my calculations I have not thought it necessary to carry the fractions beyond the first decimal.

discrepance arises from the fact that he has taken account only of those cases (seven) which present *histological* changes.¹ It is a bad rule, however, which does not work both ways, as the old proverb tells us, and so we can not help thinking, since he uses the percentages of "changes" in the ciliary nerves, and in the retina and optic nerve, for comparison, that it would have been better for him to follow the same plan in obtaining the former that he adopted in calculating the latter. This, however, has not been done, for the 79 per cent. of changes in the retina and optic nerve, which he gives, includes the many cases in which only gross changes (chiefly detachment) of the retina are described. Moreover, although no intimation is given of the fact, the $16\frac{2}{3}$ per cent. of changes in the ciliary nerves has reference to only the forty-three cases in which their histological condition is mentioned, while the 79 per cent. of retinal and optic-nerve changes refers to the whole series of one hundred and ten (as given by him) cases. Furthermore, he certainly does not mean what he says, when he speaks of 79 per cent. of the eyes exhibiting changes in the "optic nerve *and* retina,"² for a careful survey of the table shows that only 27, or 24.1 per cent. of the one hundred and twelve eyes, exhibit changes in *both* the retina and optic nerve. The condition of the retina itself is mentioned in eighty-one cases; once it is spoken of as "wanting," and in every other instance pathological changes, either histological or gross, are described, partial or complete detachment being named 63 times. That is to say, the retina is in an abnormal condition in 100 per cent. of the cases in which its state is referred to, or 72.3 per cent. of the whole number of eyes. The optic nerve is mentioned 32 times, or in 28.5 per cent. of the cases, pathological changes—including atrophy 14 times, and optic neuritis 6 times—being described in each instance. In 76.7 per cent. of the cases (or upon his basis of 110 eyes in 78.1 per cent.) pathological changes affecting either the retina or optic nerve, or both, are found, and it is to this, probably, that the 79 per cent. of changes

¹ As he states on p. 472.

² *Op. cit.*, pp. 472 and 474. *Italics* my own.

in the optic nerve *and* retina, as he expresses it, refers. Had he followed the same rule in regard to the optic nerve and retina that he did with the ciliary nerves, and taken account only of those cases in which *histological* alterations are mentioned, his percentage of pathological changes would have been reduced from 79 to about 40.

A striking contrast, as regards the condition of the ciliary nerves, is brought out, if we group separately Alt's own cases, and those which he has taken from literature. Thus, in the 31 cases of his own in which the ciliary nerves are mentioned, they are described as normal 26 times, or in 83.8 per cent. of the eyes, and as presenting histological or gross pathological changes 5 times, or in only 16.1 per cent.; while in the 15 cases from literature in which they are spoken of, they are described as normal in but 33 $\frac{1}{3}$ per cent. of the eyes, and as pathological in 66 $\frac{2}{3}$ per cent.

In the ARCHIVES OF OPHTHALMOLOGY, September, 1881,¹ Dr. W. C. Ayres, of New York, gives the notes of 4 eyes enucleated for sympathetic inflammation, and 3 for sympathetic irritation, which he examined microscopically, and in every one of which he discovered pathological changes in the ciliary nerves. If we add these to the 15 cases taken from literature by Alt, we have a total of 22 cases, in which the ciliary nerves are pathological 17 times, or in 77.2 per cent., and normal only 5 times, or in 22.7 per cent. In the same paper there is reported also a case in which an eye containing a gun-cap was enucleated for iridocyclitis purulenta. In this instance the fellow-eye "had manifested *no sympathy*, and the examination of the enucleated eye revealed the very significant fact "that every [ciliary] nerve-bundle * * * examined was completely degenerated, and divided somewhere in its course by accumulations of small round cells."

The next point worthy of comment is, that Alt should have found the ciliary nerves histologically normal (and showing gross pathological changes but twice) in fourteen of the fifteen eyes enucleated on account of sympathetic

¹ Vol. x., No. 3, p. 277 *et seq.*

irritation, which were submitted to him for examination, their condition in the one remaining eye not being mentioned. Here, it seems to me, he is unfortunate in proving too much; for even the most uncompromising opponent of the doctrine that sympathetic *inflammation* is transmitted through the medium of the ciliary nerves, admits, at least, that sympathetic *irritation* is propagated in this way. So that we are forced to conclude, either that an eye in which the ciliary nerves are entirely normal may excite sympathetic irritation of such serious character as to justify its enucleation; or else, what is much more likely, that pathological changes capable of causing such sympathetic symptoms may exist in the ciliary nerves of the exciting eye (affecting most probably not their trunks, but their terminal filaments in the iris and ciliary body), and yet be entirely undetectable with the microscope.

As to the 79 per cent. of pathological changes in the "retina and optic nerve," to which Alt and those who quote his statistics attach so much importance, they are clearly of little significance in so far as they have any bearing upon the question of the mode of transmission of sympathetic ophthalmia. In the first place, it is manifest that almost every eye in which these changes were discovered had been the seat of disorganizing inflammation, which had, indeed, involved the retina and optic nerve, but only in common with all the other important structures of the eye, including the iris, ciliary body, choroid, lens, and vitreous humor. Indeed, Alt himself admits¹ that in the whole series of cases there is but one "in which there was an affection of the retina without coincident affection of the uveal tract." In the second place, when we examine into the character of the changes which go to make up the total of 79 per cent. (as given by Alt, but 76.7 per cent. according to my calculation), we find that in a large majority of the cases they consist in detachment of the retina, or in atrophy or excavation of the optic nerve, optic neuritis and retinitis being mentioned each but six times, and being concurrent, moreover, in five instances. That detachment of the

¹ On p. 474.

retina, by causing traction upon the ciliary body, might influence the development of sympathetic ophthalmia (supposing that it is propagated through the ciliary nerves), may readily be believed, but it will scarcely be maintained that it could do so, if the hypothesis that the sympathetic affection is the result of a progressive optic neuritis be accepted as correct. And it is quite as manifest that the excavated and atrophic optic nerves, which figure so frequently in the tables, are incapable of producing such a result. If it be urged that the atrophy indicates antecedent neuritis, it may be said, in reply, that the condition of optic-nerve atrophy occurs with especial frequency in the eyes which were enucleated on account of sympathetic *irritation*; so that in these cases, at least, the neuritis must have run its course, and disappeared, without the inflammation having extended to the second eye. With these three classes of cases thrown out, the percentage of retinal or optic-nerve changes, dwindles into insignificance, especially when the graver pathological alterations with which these changes were in almost every instance associated are taken into account.

No! If we would discover the true significance of Alt's statistics, we must not look to the data bearing upon the condition of the optic nerve and the retina, but to those which have reference to the cornea, iris, and ciliary body. Here we meet with the old familiar story—iritis and cyclitis, plastic or purulent, recurring again and again; foreign bodies in the ciliary region; corneal wounds with incarceration of iris; sclerotic wounds with involvement of ciliary body;—these are the conditions which are enumerated in an almost unbroken series from the beginning to the end of his tables. Only once in the whole series of one hundred and twelve cases is evidence wanting of the uveal tract being the seat of pathological changes,¹ and but for the scantiness of the information given in regard to this case (in which there seems to have been a gunshot wound of the eye), even this single exception would probably not have to be noted.

¹ Waldeyer's Case (31), p. 426.

In a word, we fail to find any justification, whatever, for the conclusion reached by Alt (and which has been accepted by so many), that the data he has brought together strongly sustain the view that the optic nerve plays an important part in the transmission of sympathetic ophthalmia; but, on the contrary, we are convinced that if his statistics be examined in an unbiassed spirit it will be found that it is the old theory, which attributes to the ciliary nerves the important part in the production of sympathetic ophthalmia, that is, in reality, "strongly sustained."

As to the *clinical* evidence which has been relied upon to support the view that sympathetic ophthalmitis is the result of a progressive optic neuritis which extends from the primarily to the secondarily affected eye, it proves upon examination to be as inconclusive as the pathological testimony which we have just examined. Vose Solomon and Mooren, for example, each report a case in which sympathetic inflammation appeared after enucleation of the exciting eye, and as they had the misfortune to employ defective scissors to divide the optic nerve with, they rush to the absurd conclusion that the sympathetic affection was due to the bruising of the optic-nerve fibres, and hence that the inflammation must have spread by this route. It is scarcely necessary to point out, as Brudenell Carter has already done in alluding to Solomon's case,¹ that the ciliary nerves must have participated in the unusual laceration to which the optic nerve was subjected; so that as far as the question of transmission is concerned, these cases are without significance, and may be quoted with the same show of reason in support of either the ciliary-nerve or the optic-nerve hypothesis. It may be remarked also in regard to these cases, as well as of the frequently quoted cases of Colsmann and Hugo Müller (in which a neuro-retinitis developed in the uninjured eye a few days after the enucleation of the other), that not only is there no ground for supposing that the sympathetic outbreak was in any way dependent upon the *cutting of the optic nerve*, but that it is not improbable that the attack would have occurred, exactly

¹ "Diseases of the Eye," Am. edition, p. 115.

as it did, had the exciting eye not been enucleated. Indeed, it would be entirely unjustifiable to assume, in the cases of Colsmann and Hugo Müller, that the operation bore any such relation to the inflammatory outbreak in the second eye as usually exists between a traumatism of an eye and the sympathetic disease which it induces, because of the briefness of the interval that separated the two events. The most that can be claimed is, that the sympathetic attack, which was imminent, was precipitated by the shock of the operation; and admitting this, it seems much more likely that the determining influence was transmitted through the ciliary nerves than through the optic. As to the interesting case reported by S. C. Ayres,¹ in which a sympathetic inflammation that had made its appearance some time after enucleation of the other eye was cured by resection of the optic-nerve stump, it is evident, since the patient suffered severe and persistent pain in the empty socket, which certainly could not have been dependent upon irritation of a nerve of special sense, such as the optic, that some of the orbital branches of the fifth nerve, probably the remains of the ciliary nerves which had become involved in the cicatricial tissue about the optic-nerve stump, were in a pathological condition; and it is equally certain, since the resection relieved both the pain and the sympathetic inflammation, that it included these branches as well as the extremity of the optic nerve. Probably a condition existed here not unlike that which Dr. Poncet found on enucleating an eye for sympathetic mischief, upon which an optico-ciliary neurectomy had been previously performed without beneficial effect. The case was reported by him to the Ophthalmological Section of the International Medical Congress, London, 1881. The ciliary nerves were embedded in a dense mass of cicatricial tissue, which had formed about the posterior pole of the eye as a consequence of the previous operation, and exhibited marked inflammatory changes. In commenting upon the features of this case, Dr. Poncet alluded to the possibility of a similar condition occurring after enucleation, and suggested that the devel-

¹ ARCHIVES OF OPHTHALMOLOGY, vol. xi., No. 2, p. 199.

opment of sympathetic inflammation after removal of the exciting eye might be explained in this way.¹ Upon this point Mauthner remarks: "I think that in every case in which we have been obliged to ascribe the outbreak of sympathetic symptoms to the enucleation itself, or to the introduction of an artificial eye, we have, so far, observed that the region in the bottom of the orbit which was occupied by the stump of the excised nerve, and its accompanying ciliary nerves, was sensitive to the touch, as well as that the conjunctiva lining the cavity was swollen, red, and painful."²

But, even supposing there are no evidences of inflammation in any of the orbital branches of the fifth nerve, it is still quite unnecessary to adopt the progressive optic neuritis hypothesis in order to account for the origin of sympathetic inflammation, or the persistence of sympathetic irritation, after enucleation of the exciting eye; for it is altogether probable that the disturbances of nutrition in the second eye are preceded by, and are dependent upon, molecular alterations (perhaps a slight myelitis, as suggested by Brecht) in the vaso-motor or "trophic" centres, and that these again are secondary to alterations of similar character in the Gasserian and ophthalmic ganglia; so that we need only suppose that in exceptional instances these changes have progressed so far as not to be arrested by the enucleation of the eye, to obtain an entirely satisfactory explanation of the etiology of these anomalous cases.

The occasional occurrence of sympathetic "*neuro-retinitis*" is urged as an additional argument in favor of the view that the optic nerve is the route by which the inflammation reaches the second eye. It is worthy of remark, however, that it is always a *neuro-retinitis*, and never a pure *neuritis* or *papillitis*, that is spoken of. Mauthner refers to a number of cases of sympathetic choroido-retinitis, a few cases of retinitis, and a still smaller number diagnosed as *neuro-retinitis*; but, though he devotes a paragraph to "sympathetic af-

¹ See Transactions of the Seventh International Medical Congress, vol. iii, p. 39.

² "Sympathetic Diseases of the Eye," Mauthner, English translation, p. 136.

fections of the optic nerve,"¹ he alludes only to a few doubtful cases of simple atrophy, and makes no mention whatever of neuritis. It is safe to say, I think, that no case of sympathetic optic neuritis has yet been recorded in which there were not indications of the coexistence of inflammation of at least the adjacent portions of the choroid and retina. Now, it is well known that an intimate anastomosis exists between the blood-vessels of the optic disc and those of the surrounding choroid, and that hyperæmia of the former and indistinctness of its outline frequently accompany even the slightest grades of choroiditis. It is also known that the short ciliary nerves, which enter the eyeball around and in close proximity to the optic nerve, give off many branches to the neighboring choroid—in fact, that the posterior segment of the choroid is especially rich in its ciliary-nerve supply.² That sympathetic inflammation, therefore, which usually commences as an irido-cyclitis, should occasionally begin as a posterior polar choroiditis, the inflammation quickly involving the retina and optic nerve, is exactly what we might expect, if it be dependent upon an influence reflected through the ciliary nerves; and this, we believe, is the true explanation of most, if not all, of the cases of so-called neuro retinitis of which we have of late heard so much.³

A further objection which may be urged against the theory of a progressive optic neuritis is this: If the inflammation which has spread from the exciting eye reaches the second eye as a simple descending neuritis, we should expect only such results as usually follow neuritis of this character, that is to say, ultimate atrophy, perhaps, of the optic nerve and retina, but little, if any, implication of the uveal tract, certainly none of its anterior portion—the ciliary

¹ *Op. cit.*, p. 92.

² H. Müller, Schweigger, Stellwag, Pope, etc. See "Anatomy and Histology of the Human Eye," Metz, p. 39.

³ Even a pure sympathetic neuritis might, of course, be produced by a reflex influence dependent upon irritation of the ciliary nerves. Anatomists (Hirzel and Tiedemann) assert that a twig from the ophthalmic ganglion enters the optic nerve with the arteria centralis retinæ. In view of this fact, we should heed the advice which Alt gives (upon other grounds), to remove a large piece of the optic nerve when we enucleate an eye for present or threatening sympathetic disease.

body and iris. It is scarcely necessary to say, however, that such is not the case, but that even when the inflammation commences at the posterior pole of the eye, it usually spreads to the anterior portion of the uveal tract, and terminates in a malignant irido-cyclitis.

In regard to the case of sympathetic iritis reported by Alt in the ARCHIVES OF OPHTHALMOLOGY, vol. viii, No. 1, in which he thinks the inflammation was "mechanically" transmitted to the second eye by way of the optic nerve, because there was found in the enucleated eye "a very active inflammatory process in the optic nerve and retina, while the ciliary nerves appeared perfectly unaltered,"¹ we think it would be difficult for him to explain, in accordance with this view, how the inflammation reached the iris of the second eye; and still more difficult to explain how, when it had reached this point by "mechanical extension," it was arrested, as he claims it undoubtedly was, by the enucleation of the other eye. On the other hand, these difficulties at once disappear, if we assume that the influence which determined the development of the iritis in the second eye was reflected through the ciliary nerves, and was dependent upon an irritation of their terminal filaments in the inflamed iris and ciliary body of the exciting eye, the normal condition of their trunks in this eye being, in fact, conducive to such reflected action; for not only is the question of the origin and location of the sympathetic inflammation disposed of at once, but we are enabled to comprehend how the enucleation of the primarily affected eye favorably influenced the condition of the fellow-organ, by relieving it of a continuously acting source of irritation.

The influence which *the germ theory of disease* has exerted upon the question of the pathogeny of sympathetic ophthalmia, to which reference has been made, is exhibited in the now-popular septic choroiditis and perineural lymph-space doctrine advanced by Leber, and advocated, notably, by Snellen, before the Ophthalmological Section of the London International Medical Congress, (1881). Concerning this

¹Page 106.

doctrine, which regards sympathetic ophthalmitis as *an inflammation of septic character, that has spread from the primarily to the secondarily affected eye by way of the inter-vaginal lymph-space of the optic nerve*, it is to be said: that the evidence adduced in its favor is extremely meagre; that the arguments by which it is supported are inconclusive; and that, at best, it is of but limited application. Leber, for example, adopts this theory mainly in consequence of having found pronounced hyperplasia of the inter-vaginal connective tissue of the optic nerve, with proliferation of the endothelium, in four eyes enucleated for sympathetic trouble¹; and Snellen, though he points out how the coincidence of an infective plastic inflammation of the uveal tissue, with closure of the anterior and dilatation of the posterior lymphatic spaces of the eye, might produce such septic transference, has little additional testimony to offer, beyond the statement that the tension of the exciting eye constantly increases before the second eye is affected, and his observation, in a freshly prepared microscopic specimen from an eye just enucleated on account of a serious traumatism received three weeks previously, of a mass of moving molecules, which were presently recognized as being for the most part pigment molecules from the uveal tissue, though "several somewhat larger bodies showed by their ampler movements all the characteristics of micrococci."² The former argues that the pertinacity of sympathetic ophthalmitis, its frequent relapses, and its involvement of so many different parts of the eye, render probable its infectious origin; but this certainly is an unwarrantable conclusion, since the severer forms of herpes zoster ophthalmicus (which is perhaps more nearly related to sympathetic inflammation, and in some respects resembles it more closely, than any other variety of ophthalmia) present just such characteristics. The occasional occurrence of sympathetic inflammation after enucleation of the exciting eye, he also alludes to as having a similar bearing; but of this we

¹ *Archiv für Ophthalmologie*, vol. xxvii, 1, p. 325 *et seq.*

² Transactions of the International Medical Congress, Seventh Session, London, 1881, vol. iii. p. 31 *et seq.*

have already spoken, giving it quite a different interpretation.

The first and most obvious objection to this doctrine (which Leber himself appreciates) is, that sympathetic inflammation almost always begins in the anterior portion of the uveal tract, and not in the region of the optic nerve, as should be the case if this view were correct. Leber, indeed, suggests that neuritis may always be present without being recognized, owing to the turbidity of the vitreous humor; but, as the neuritis should manifest itself first, it ought to be more frequently observed before the inflammatory process has extended to the uveal coat and rendered the media cloudy. Indeed, if there be any truth in Leber's other theory, that papillitis, or choked disc, is dependent upon the presence of a phlogogenic fluid in the optic-nerve intervaginal space,¹ then, if his view of the etiology of sympathetic ophthalmia were correct, it would seem that just this condition of a well-marked neuritis should be the most frequently met with and the most characteristic feature of the disease; but, as has been said, papillitis, or choked disc, appears to be the one form of sympathetic inflammation which has not been recorded. Moreover, if papillitis and sympathetic ophthalmitis resemble each other as closely in their etiology as Leber would have us believe, it seems not impertinent to inquire why they should differ so absolutely in their clinical history. Again, it may be said, that if the description usually given by anatomists of the intervaginal space of the optic nerve be correct, namely, that it ends abruptly in the sclerotic tissue about the optic-nerve entrance, being cut off from the deeper tissues of the eye by the interposition of the pial sheath, which at this point turns out to blend with the inner third of the sclerotic, the dural sheath being lost in the outer two thirds, it is difficult to understand how the inflammatory process spreads hence to the ciliary body and iris. Some authorities claim that there are lymph-spaces in the lamina cribrosa which communicate directly with the intervaginal space, but this Leber, himself, has denied.² The occurrence of dropsy of the

¹ *Op. cit.*, p. 52 *et seq.*

² Trans. Seventh International Med. Congress, (1881), vol. iii., p. 55.

intervaginal space, with distention of the ocular end of the nerve-sheath, seems also to indicate the absence of any direct communication between this cavity and the interior of the eye.¹

Another serious objection to this theory is, that in many instances the condition of the exciting eye, at the time of the sympathetic outbreak, is not such as to warrant the assumption that it is the seat of a plastic or septic uveitis. I have already alluded to a case in my own experience, in which a sympathetic neuro-retinitis (or more accurately, perhaps, a posterior polar choroido-retinitis) developed in consequence of a very severe and obstinate traumatic keratitis of the opposite eye. The corneal inflammation was caused by the instillation into the eye of aqua ammonia, which had been mistaken for a collyrium, and, although for months the keratitis persisted, and the eye remained extremely irritable and photophobic, there was certainly at no time any serious implication of the uveal tract. My notes show that a short while before the sympathetic inflammation made its appearance, the vision of the injured eye was tested, and that, in spite of a very considerable amount of corneal cloudiness and irregular astigmatism, the patient was able to read with it J. No. 8. The irritability of this eye gradually disappeared, and after a protracted treatment, which consisted chiefly in the administration of iodide of potassium and biniodide of mercury, and the application of the artificial leech, the sympathetic inflammation slowly subsided.²

The irritation caused by the incarceration of a tag of iris in a corneal scar, as in the now discredited operation of

¹ Dr. Win. F. Norris, of Philadelphia, using the bodies of young children, succeeded without difficulty in filling the intervaginal space of the optic nerves by injecting fluids through the anterior fontanelle into the subarachnoid space. But, though his injections "filled also the lymph-spaces of the spinal cord and of the nerves given off by it," only in a few instances, "with high pressure," did they penetrate from the subdural to the perichoroidal space.—*Phila. Med. Times*, vol. ix., p. 567.

² Brailey, speaking of the possibility of sympathetic inflammation travelling along the intervaginal space, states, "that the inflammation of this is usually extremely slight, compared with that of the uveal tract itself, and that sympathetic inflammation may occur without any implication of the choroid in the neighborhood of the papilla of either eye." *Trans. Seventh International Med. Congress (1881)*, vol. iii., p. 38.

iridodesis, has not infrequently provoked a sympathetic ophthalmitis, without exciting in the primary eye a serious amount of inflammation¹; and a shrunken stump, in which all inflammation that could possibly be regarded as of infectious character had long since subsided, has often done the same.

Lastly, it may be said, that there is one well-recognized form of septic inflammation of the uveal tract—suppurative or metastatic choroiditis,—and that the clinical history which it presents is wholly unlike that of sympathetic inflammation. In order to fortify his theory Leber attempts to explain the well-known fact that suppurative panophthalmitis rarely gives rise to sympathetic inflammation, by assuming that the septic germs “are partly gotten rid of by purulent perforation of the eyeball, and partly destroyed or rendered inert by enormous development of pus.” I submit, however, that the etiology of this disease, and the consequences which not infrequently flow from it, prove it to be the typical infectious ophthalmitis, and that it, above all other forms of ocular inflammation, would be most apt to excite sympathetic ophthalmia, were the theory of its pathogeny which Leber has promulgated true.

Finally, to the many, ever ready to follow each swing of the pendulum of popularity, who would cast aside as of no value all that clinical observation has taught us concerning the pathogeny of sympathetic ophthalmia, *because it happens not to harmonize with the latest dictum of the latest school of pathology*, I would say: that though the predominant school of pathology at the present day may busy itself but little with the influence which the nerves may exert upon inflammation, as Mauthner remarks, it is certainly not in a position to demonstrate that no such influence is exerted; and that while the experiments of Professor Ludwig, showing that the chorda tympani conveys to the submaxillary gland a specific stimulus to secretion, re-

¹ Compare “Sympathetic Diseases of the Eye,” Mauthner, English translation, p. 48.

move all *a priori* objection to the theory that inflammatory changes of texture may be produced by centrifugal "trophic" nerves,¹ there are many clinical facts, beside the almost convincing ones which the phenomena of sympathetic ophthalmia furnish, that go far to prove that either through "trophic" or vaso-motor fibres, or through both, nerve influence does determine such tissue changes.² I would also remind them, that though it is the fashion of the day to accept as conclusive the well-known experiments by which Snellen supposed he had demonstrated that the sloughing of the cornea which follows division of the trigeminus is a traumatic, and not a neuro-paralytic phenomenon, others (Samuel, Meissner, Schiff) have experimented in this same field, and have obtained results which led them to adopt directly opposite views; and that so close an observer and logical a reasoner as Von Graefe rejected absolutely Snellen's conclusions, (as very many ophthalmologists have done since,) because he found them opposed to facts with which his clinical experience brought him into daily contact;³ also, that in the reports of nearly all eye hospitals there are recorded cases of neuro-paralytic keratitis, and that within the past few years ophthalmic surgeons have shown a disposition to attach more and more importance to diseases of this type—diseases, as Brudenell Carter aptly expresses it, which are essentially neuropathic in their character, and differ from neuralgia chiefly in this

¹See article on Inflammation in "Holmes' System of Surgery," vol. I., p. 90.

² Among the most striking may be mentioned the well-known observations recorded by Mitchell, Morehouse, and Keen,) Gunshot Wounds and other Injuries of Nerves, Phila., 1864; Circular No. 6, Surgeon-General's Office, 1864); the cases of reflex structural changes due to dental disease, described in Guy's Hospital Reports (third series, vol. xiii.) by Mr. Salter; and the ulceration of the duodenum which occurs so frequently in consequence of extensive burns of the surface of the body, and which Brown-Séquard succeeded also in producing experimentally. The statement of Mooren that he has seen cases of optic neuritis which were dependent upon uterine displacement, and which disappeared when this was corrected, may also be mentioned in this connection.

³One can readily believe that the corneal inflammation and ulceration that supervene upon division of the trigeminus might be favorably modified by keeping the lids closed over the eye; but the suggestion that the ulcerative and necrotic changes which result in the destruction of the cornea within forty-eight or seventy-two hours after the section of the nerve are due simply to the injury to which the eye is exposed, owing to its anæsthetic condition, seems preposterous. Certainly, if we may reverse the usual order, and reason from man to the rodentia, we should be warranted in so regarding it.

respect, that they declare themselves by abnormal tissue change instead of by abnormal sensation.¹ And, lastly, I would point out to them, that though the pathologists of the Cohnheim school contend that the reflex congestion which follows stimulation of sensory nerves is not inflammation, and does not lead directly to it, they admit that when this condition has existed for some time (as in the premonitory stage of sympathetic ophthalmia) it places the cells of the part in a condition of instability, lowers the vitality of the capillary walls, and offers facilities for the emigration of leucocytes ; so that at any moment, upon the slightest provocation, (in the case of the eye, for example, from the irritation caused by overwork or undue exposure to light²) inflammatory changes may be precipitated.³ So that, after all, they may accept the Cohnheim doctrine in its entirety, and at the same time, without being illogical, they may believe what clinical evidence so plainly declares—that sympathetic ophthalmitis is dependent, if not directly, at least secondarily, upon a reflex influence transmitted through the ciliary nerves.

Briefly summarized the conclusions which seem to me to be warranted by the facts we have examined are :

1st. That the doctrine that sympathetic ophthalmia is the result of a progressive optic neuritis, which spreads from the primarily to the secondarily affected eye, is supported by no facts worthy of serious consideration, but is the out-

¹ "Diseases of the Eye," Am. edition, p. 113. Also compare Noyes : "Diseases of the Eye," p. 190 ; and see an interesting article in the *Am. Journal Med. Sciences*, July, 1881, by Dr. Jas. L. Minor : Anæsthesia of the Cornea, and its Significance in Certain Forms of Eye Disease, in which he makes the significant statement that "*anæsthesia of the cornea existed in six [of his] cases without keratitis ; and in those cases that presented both anæsthesia and inflammation, complete protection of the eye did not materially alter the course of the disease.*"

² Brailey (Trans. London Med. Congress, 1881, vol. iii., p. 38) mentions that sympathetic inflammation frequently occurs shortly after patients leave the hospital ; and he attributes this to the exposure of the second eye to light. He also states that the records of Moorfield's Hospital "show that a wound occurring in the summer months is more liable than one in the winter to be followed by sympathetic disease" and "that sympathetic inflammation is more likely to break out in summer, irrespective of the time when the first eye was injured."

³ See the very interesting (Bradshaw) lecture on The Influence of the Sympathetic on Disease, by Dr. Edward Long Fox, *British Med. Journal*, Aug. 26, Sep. 2, 1882.

growth of grossly misinterpreted clinical and pathologico-anatomical observations.

2d. That the septic choroiditis theory of Leber rests upon evidence which is scarcely more substantial ; and from both an anatomical and a clinical point of view is open to serious objection.

3d. That there is an overwhelming preponderance of testimony, both clinical and pathologico-anatomical (which, however, for obvious reasons, it has been the fashion of late to systematically belittle), in favor of the one-at time universally accepted doctrine that sympathetic ophthalmitis, like sympathetic irritation, is a reflex neurosis, dependent upon irritation of the ciliary nerves of the exciting eye (probably for the most part of their terminal filaments in the ciliary body and iris)¹ ; and that as this testimony goes far to show that inflammatory changes of texture, as well as abnormalities of sensation, may be produced by reflex nerve influence, it has a very important bearing upon the theory of the etiology of inflammation at present most in favor.

4th. That, as the history of the last quarter of a century plainly shows, experimental pathologists, as well as clinicians, are liable to fall into error, and that for this reason it behooves the latter to be less eager to cast aside as untrustworthy the lessons they have learned from the daily observation of disease, because they may seem to conflict with the dicta which the laboratories from time to time give forth.

¹ That in some instances inflammatory changes occur in the second eye without well-marked sympathetic irritation, and that in others sympathetic irritation of the most marked character exists for a long time without inflammation, does not militate against the view that both of these conditions are dependent upon a reflex influence transmitted through the ciliary nerves, as some would have us believe. In the first place, the ciliary nerves contain sympathetic as well as sensory fibres, and it is probable that the former have most to do with trophic changes, the latter with disturbances of sensation. In the second place, in view of the astonishing difference in the degree of pain inflicted in different persons by the same amount of violence done to the nerves, we are justified in assuming that in the eye, as well as in other parts of the body, these two kinds of fibres do not always exist in the same relative proportion, or, at least, that in different individuals, sometimes the influence of one set, and sometimes the influence of the other, may predominate. Admitting this much, we shall have no difficulty in comprehending why a given lesion of the ciliary body, for example, should give rise, in one instance, to pronounced sympathetic irritation unaccompanied by structural changes ; and in another, to trophic changes in the sympathizing eye with little or no accompanying irritation.

